

Serial No. 10/091,912

Page 6

REMARKS

The present application was originally filed with 29 Claims. In a Restriction Requirement mailed November 18, 2003, the Examiner restricted the Claims into 12 Groups:

Group I: Claims 1-4, 17, 28, and 29, drawn to a cutinase variant having a substitution of Gly at position 59 of SEQ ID NO:2;

Group II: Claims 1-3, 5, 24, 28, and 29, drawn to a cutinase variant having a substitution of Thr at position 177 of SEQ ID NO:2;

Group III: Claims 1-3, 6, 25, 28, and 29, drawn to a cutinase variant having a substitution of Thr at position 64 of SEQ ID NO:2;

Group IV: Claims 1-3, 7, 28, and 29, drawn to a cutinase variant having a substitution of Tyr at position 150 of SEQ ID NO:2;

Group V: Claims 1-3, 8, 26, 28, and 29, drawn to a cutinase variant having a substitution of Tyr at position 182 of SEQ ID NO:2;

Group VI: Claims 1-3, 9-10, 12-16, 19, and 27-29, drawn to a cutinase variant having a substitution of Phe at position 180, Ser at position 205, and Ile at position 178 of SEQ ID NO:2;

Group VII: Claims 1-3, 11, 28, and 29, drawn to a cutinase variant having a substitution of Gly at position 61 of SEQ ID NO:2;

Group IX: Claims 1-3, 20, 28, and 29, drawn to a cutinase variant having a substitution of Arg at position 20, and Tyr at position 112 of SEQ ID NO:2;

Group X: Claims 1-3, 21, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 205 and Phe at position 207 of SEQ ID NO:2;

Group XI: Claims 1-3, 22, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 63 of SEQ ID NO:2; and

Group XII: Claims 1-3, 23, 28, and 29, drawn to a cutinase variant having a substitution of Ser at position 85 of SEQ ID NO:2

The Examiner argued that the Groups represent separate and patentably distinct inventions. In a Response filed December 16, 2003, Applicants respectfully traversed the restriction requirement and elected the Claims in Group VI (Claims 1-3, 9-10, 12-16, 19, and 27-29, drawn to a cutinase variant having a substitution of Phe at position 180, Ser at position 205, and Ile at position 178 of SEQ ID NO:2). Applicants withdrew Claims 4-8, 11, 17-18, and 20-26, as being drawn to a non-elected invention. In the prior Office Action (dated January 29,

GC724 Final OA Response 9-27-04

Serial No. 10/091,912
Page 7

2004), the Examiner made the Restriction final. In the Response filed on July 15, 2004, Applicants cancelled Claims 4-8, 17-18, and 20-26. In order to avoid any additional confusion, Applicants also cancelled Claims 12-16, in order to correct the inadvertent omission of Claim 12 in the Response filed December 12, 2003. New Claims 34-38 filed in the Response correspond to Claims 12-16 with amendments to correct sentence structure.

Applicants appreciatively note that the Examiner has removed a number of the previous objections and rejections. The Examiner has objected to Claims 1, 19, 27-28, 30-31, and 33-38, as the identification of amino acid residues/positions is inconsistent. The Examiner has suggested that the Claims be consistent in identifying amino acids throughout the Claims. Applicants have amended the Claims to consistently recite the residues/positions. In addition, Claims 1 and 28 have been amended such that the sites are listed in numerical order.

In addition, the Examiner has objected to Claims 2 and 29 as allegedly failing to further limit the subject matter of the independent Claim. Applicants must respectfully disagree with the Examiner's argument, as Claims 1 and 28 are broader than corresponding Claims 2 and 29, in that Claims 1 and 28 encompass cutinases obtained from organisms other than *P. mendocina*. In contrast, Claim 2 is limited to cutinases obtained from *P. mendocina* and Claim 29 is limited to cutinases obtained from *Pseudomonas* species.

In addition, the Examiner objected to Claim 37 for the recitation of "Phy 194," which was indeed a typographical error. As this recitation has been deleted, Applicants respectfully submit that this Claim is in proper form.

The Examiner's rejections are addressed below in the following order:

- 1) Claims 27 and 28 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite;
- 2) Claims 1-2, 9, 19, and 27-38 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 3) Claims 1-2, 9, 19, and 27-38 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled;
- 4) Claims 1-2, 9, and 27-38 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Poulouse *et al.*

Serial No. 10/091,912
Page 8

1) The Claims are Definite

The Examiner has rejected Claims 27 and 28 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants must respectfully disagree.

The Examiner argues that Claims 27 and 28 are indefinite in the recitation of "stability." Although Applicants believe that there is more than sufficient support in the Specification as filed for these recitations, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Claim 27 has been amended to recite "thermostability," and Claim 28 has been amended to recite that the cutinase variant is more thermostable than wild-type cutinase. Applicants reserve the right to pursue the original and/or other related Claims in subsequent filing(s). As the Claims are definite, Applicants respectfully request that this rejection be withdrawn.

2) The Written Description is Met

The Examiner has rejected Claims 1-2, 9, 19, and 27-38, under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement. In particular, the Examiner argues that the Claims "encompass a widely variant genus with respect to the amino acid sequences of the claimed genus of cutinase variants, including any variant having any combination of substitutions of the reference sequence of SEQ ID NO:2." (Final Office Action, page 6). Applicants must respectfully disagree, as the Claims limit the genus to variants having substitutions at positions 192 and/or 194, and in some Claims, at position 219. In view of the fact that the Specification provides a number of representative species. Applicants must respectfully disagree with the Examiner's arguments, as Applicants have clearly disclosed additional species of cutinase variants, as indicated by the data provided in Table 1 (page 14). In this Table, data for polyesterase activity and thermostability of numerous cutinase variants are provided. Thus, Applicants have provided numerous cutinase variants. Indeed, in Table 14 alone, data are provided for cutinase variants with substitutions at 41 different positions. In view of this, Applicants respectfully submit that there are many more representative species provided in the Specification as filed than the Examiner has recognized. Thus, Applicants respectfully submit that the written description requirement is met and request that this rejection be withdrawn.

Serial No. 10/091,912

Page 9

3) The Claims are Enabled

The Examiner has rejected Claims 1-2, 9, 19, and 27-38, under 35 U.S.C. §112, first paragraph, as allegedly not being enabled. The Examiner admits that the Specification is enabling for SEQ ID NO:2 with substitutions at positions 192, 194, and 219. However, the Examiner argues that the Specification does not provide enablement for other substitutions. As indicated above, Applicants must respectfully disagree, as many more cutinase variants are indeed provided by the Specification as filed. Thus, in contrast to the Examiner's assertions, the present Specification enables many cutinase variants in addition to those specifically recited in the Claims as having substitutions at positions 192, 194 and 219 of SEQ ID NO:2. The Specification provides means to test cutinase variants having substitutions at positions 192, 194, and/or 219, in addition to these substitutions in combination with other substitutions. As the present Specification provides numerous examples of cutinase variants having the required substitutions (*i.e.*, 192 and/or 194 and/or 219), as well as means to identify variants that are encompassed by the Claims, Applicants respectfully submit that the Claims are enabled. As the Claims are enabled, Applicants respectfully request that this rejection be withdrawn.

4) The Claims are Unobvious

The Examiner has rejected Claims 1-2, 9, and 27-38 under 35 U.S.C. §103(a) as allegedly being unpatentable over Poulouse *et al.* (U.S. Patent No. 5,352,594). In particular, the Examiner argues that "Poulouse [sic] et al. teach variants of a *P. mendocina* lipase (columns 3-5) having substitution of Ser205 (corresponding to amino acid 219 of SEQ ID NO:2) with various amino acids (see columns 11-14). Poulouse [sic] et al. further teach that the catalytic triad of *P. mendocina* lipase is Ser126, His208, and Asp176 (column 5, middle)—corresponding to amino acids Ser140, His220, and Asp190 of SEQ ID NO:2, and that replacement of amino acid within about 6 amino acids N- or C-terminal to a catalytic amino acid will lead to an increase or decrease in the perhydrolysis/hydrolysis ratio and the kinetic constraints of the enzyme (column 5, lines 41-57)." (Final Office Action, page 8).

In particular, the Examiner argues that "Poulouse et al. teach that in order to obtain an enzyme with the best ratio or substrate specificity in a desired direction, more than one amino acid substitution can be made" (Final Office Action, pages 8-9). The Examiner concludes that it would have been obvious to mutate position 178 or 180 of *P. mendocina* lipase (corresponding positions 192 and 194 of SEQ ID NO:2) or to further mutate position 180 of the *P. mendocina* lipase position 205 (corresponding to position 205 of SEQ ID NO:2) mutants of

Serial No. 10/091,912
Page 10

Poulose et al. with any amino acid." (Final Office Action, page 9). Applicants must respectfully disagree with the Examiner's arguments. In response to the Examiner's statements regarding Applicants' knowledge of the Poulose et al. Patent (US Pat. 5,352,594), Applicants knew of this Patent, but apparently inadvertently omitted it from the PTO-1449 form and Information Disclosure (IDS) filed in this case. As the Examiner has made this Patent of record, Applicants do not believe that a Supplemental IDS is required. However, Applicants will provide such a Supplemental IDS and PTO-1449, if required by the Examiner.

Applicants also note that the Examiner admits that "Poulose et al. do not teach that their *P. mendocina* esterase Ser205 variants have enhanced stability or enhanced polyesterase activity." (Final Office Action, page 10). As previously indicated, during the development of the presently claimed invention, Applicants conducted experiments using the best-performing variants as described by Poulose et al. (i.e., S205N, Q127S/S205N, and S205N/F207T) to determine their polyesterase activity. The activity of these variants was found to be unremarkable, as compared to the wild-type cutinase. As the teachings of Poulose et al. were insufficient to meet the need addressed in the present application (i.e., variants with enhanced thermostability and/or polyesterase activity), the present inventors developed the presently claimed invention in order to provide cutinase mutants with these desired properties. Should the Examiner wish to review these data, Applicants will provide them upon request.

In addition, Applicants submit that Poulose et al. teach "... one would in general use the crystal structure of the enzyme to determine which amino acids are within 15 angstroms of the active site regardless of the primary structure of the enzyme. Where no crystal structure is available, positions in the primary sequence about 6 amino acids on either side of a catalytic amino acid would be within the 15 angstrom requirement." (Poulose et al., at col. 5, lines 50-57). Applicants respectfully submit that as the catalytic triad is composed of Ser126, Asp176, and His206 (i.e., positions 140, 220, and 190 of SEQ ID NO:2), there is no teaching nor suggestion in Poulose et al. to modify the amino acids at any of these positions in order to increase the polyesterase activity and/or thermostability of the enzyme. Poulose et al. teach mutations that increase perhydrolase activity of the enzyme.

As the presently claimed invention is neither taught, suggested, nor is there any expectation of success in producing the presently claimed invention provided in Poulose et al., Applicants respectfully submit that the presently claimed invention is unobvious over Poulose et al. Therefore, Applicants respectfully request that this rejection be withdrawn.

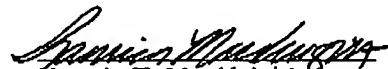
Serial No. 10/091,912
Page 11

CONCLUSION

In view of the above remarks, the Applicants believe the pending Claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

Date: December 20, 2004


Kamrin T. MacKnight
Registration No. 38,230

Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94304-1013
Tel: 650 846-5838
Fax: 650 845-6504